

## IN THE UNITED STATES PATENT &amp; TRADEMARK OFFICE

Appln. Ser. No.:	Filed:	Inventor(s):	Atty Dkt:
09/740,242	18 Dec. 2000	J. Varani	100UM-012 (1718-012)
Title: Method for Protecting and Restoring Skin Using Selective MMP Inhibitors			
Examiner: M. Williamson		Art Unit: 1616	

Asst. Comm'r for Patents  
Washington, D.C. 20231-0001

3 Pages Total **VIA FACSIMILE**  
703-746-5274

#8/A  
PKD  
7.26.02

## SUPPLEMENT RESPONSE AND AMENDMENT

Dear Sir:

In connection with the above identified application, and in supplement to the response previously filed, please amend the application as follows:

IN THE CLAIMS:

a' 1. (Amended.) A topical composition for protecting human skin from collagen degradation, comprising a compound selective for the direct inhibition of at least one of MMP-1, MMP-8, and MMP-13 being greater than the inhibition of MMP-9 and optionally also greater than the inhibition of MMP-2, and a dermatologically suitable carrier therefor.

## REMARKS

Entry of the foregoing amendments, and reexamination and reconsideration of the subject application, pursuant to and consistent with 37 C.F.R. § 1.104 and § 1.112, and in light of the following remarks, are respectfully requested.

In light of the telephonic conversation with the Examiner, and to facilitate a search of the invention, claim 1 has been amended to recite that the inhibitor is a direct-acting MMP inhibitor (as described in the specification, and as described by the Whittaker *et al.* review article). Such inhibitors are in stark contrast to the varied structures of the indirect-acting inhibitors, which can range from aspirin to retinoids to flavinoids (e.g., genistein). It should be noted that Whittaker *et al.* explain, to the extent known, the structural relationship between the compounds disclosed therein and their relative selectivity for inhibiting different MMPs.

This amendment is made without prejudice to filing a divisional application directed to the broad class of MMP inhibitors. As discussed by phone with the Examiner, only routine experimentation is necessary to determine whether any given compound is a selective MMP inhibitor as required by the claims: collagen and gelatine substrate and MMPs are commercially available through many chemical supply companies; together with the test compound, the substrate and the enzyme are mixed in a test tube, and then the substrate is examined to determine the extent (if any) by which the enzyme was inhibited.

**CERTIFICATE OF MAILING OR  
TRANSMISSION – 37 CFR 1.8**

I hereby certify that I have a reasonable basis that this paper, along with any referred to above, (i) are being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D.C. 20231, or (ii) are being transmitted to the U.S. Patent & Trademark Office in accordance with 37 CFR § 1.6(d).

DATE: 26 July 2002  
NAME: BRAD RUBEN  
SIGNATURE: Brad Ruben

Respectfully submitted,

  
Bradley N. Ruben, Reg. No. 32,058  
Bradley N. Ruben, PC  
463 First St., Suite 5A  
Hoboken, NJ 07030-1859  
201-239-0707 (fax -0734)  
mail@rubenpatent.com

26 July 2002

**APPENDIX SHOWING MARK-UPS OF AMENDMENTS**

1. (Amended.) A topical composition for protecting human skin from collagen degradation, comprising a compound selective for the direct inhibition of at least one of MMP-1, MMP-8, and MMP-13 [with respect to] being greater than the inhibition of MMP-9 and optionally also greater than the inhibition of MMP-2, and a dermatologically suitable carrier therefor.